EXHIBIT 6

CONNETICS CORP

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10–K

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Table of Contents

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10–K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Fiscal Year Ended December 31, 2004

Commission File Number 0–27406

CONNETICS CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**94–3173928**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
3160 Porter Drive	**94304**
Palo Alto, California	*(zip code)*
(Address of principal executive offices)	

Registrant's telephone number, including area code:
(650) 843–2800

Securities registered pursuant to Section 12(b) of the Act:
None

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $0.001 par value per share
Preferred Share Purchase Rights

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S–K is not contained herein, and will not be contained to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10–K or any amendment to this Form 10–K. ☑

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b–2 of the Act). Yes ☑ No ☐

The aggregate market value of the common stock held by non–affiliates of the registrant was approximately $473,000,000 as of June 30, 2004 based upon the shares outstanding and the closing sale price on the Nasdaq National Market reported for that date. The calculation excludes shares of common stock held by each officer and director of the registrant and by each person known by the registrant to beneficially own more than 5% of the registrant's outstanding common stock as of that date, in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

There were 35,926,559 shares of registrant's common stock issued and outstanding as of February 28, 2005.

DOCUMENTS INCORPORATED BY REFERENCE

The information required by Part III of this Report, to the extent that it is not set forth in this Report, is incorporated by reference to the registrant's definitive proxy statement for the Annual Meeting of Stockholders to be held on April 22, 2005.

Table of Contents

Forward–Looking Statements

Our disclosure and analysis in this Report, in other reports that we file with the Securities and Exchange Commission, in our press releases and in public statements of our officers contain forward–looking statements within the meaning of Section 27A of the Securities Act of 1933, and Section 21E of the Securities Exchange Act of 1934. Forward–looking statements give our current expectations or forecasts of future events. Forward–looking statements may turn out to be wrong. They can be affected by inaccurate assumptions or by known or unknown risks and uncertainties. Many factors mentioned in this Report — for example, governmental regulation and competition in our industry — will be important in determining future results. No forward–looking statement can be guaranteed, and actual results may vary materially from those anticipated in any forward–looking statement.

You can identify forward–looking statements by the fact that they do not relate strictly to historical or current events. They use words such as "anticipate," "estimate," "expect," "will," "may," "intend," "plan," "believe" and similar expressions in connection with discussion of future operating or financial performance. These include statements relating to future actions, prospective products or product approvals, future performance or results of current and anticipated products, sales efforts, expenses, the outcome of contingencies such as legal proceedings, and financial results.

Although we believe that our plans, intentions and expectations reflected in these forward–looking statements are reasonable, we may not achieve these plans, intentions or expectations. Forward–looking statements in this Report include, but are not limited to, those relating to the commercialization of our currently marketed products, the progress of our product development programs, developments with respect to clinical trials and the regulatory approval process, and developments relating to our sales and marketing capabilities. Actual results, performance or achievements could differ materially from those contemplated, expressed or implied by the forward–looking statements contained in this Report. In particular, this Report sets forth important factors that could cause actual results to differ materially from our forward–looking statements. These and other factors, including general economic factors and business strategies, and other factors not currently known to us, may be significant, now or in the future, and the factors set forth in this Report may affect us to a greater extent than indicated. All forward–looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by the cautionary statements set forth in this Report and in other documents that we file from time to time with the Securities and Exchange Commission including the Quarterly Reports on Form 10–Q to be filed in 2005. Except as required by law, we do not undertake any obligation to update any forward–looking statement, whether as a result of new information, future events or otherwise.

Table of Contents

PART I

Item 1. Business

THE COMPANY

References in this Report to "Connetics," "the Company," "we," "our" and "us" refer to Connetics Corporation, a Delaware corporation, and its consolidated subsidiaries. Unless the context specifically requires otherwise, these terms include Connetics Australia Pty Ltd. and Connetics Holdings Pty. Ltd. Connetics was incorporated in Delaware in February 1993, and our principal executive offices are located at 3160 Porter Drive, Palo Alto, California 94304. Our telephone number is (650) 843–2800. Connetics®, Luxíq®, OLUX®, Extina®, Soriatane®, VersaFoam® and the seven interlocking "C's" design are registered trademarks, and Evoclin™, Liquipatch™, VersaFoam–EF™, and Desilux™ are trademarks, of Connetics. Velac® is a registered trademark of Yamanouchi Europe B.V. All other trademarks or service marks appearing in this Report are the property of their respective companies. We disclaim any proprietary interest in the marks and names of others.

Connetics is a specialty pharmaceutical company that develops and commercializes products for the dermatology marketplace. This marketplace is characterized by a large patient population that is served by a relatively small, and therefore readily accessible, number of treating physicians. We currently market four pharmaceutical products, OLUX® (clobetasol propionate) Foam, 0.05%, Luxíq® (betamethasone valerate) Foam, 0.12%, Soriatane®–brand acitretin, and Evoclin™ (clindamycin) Foam, 1%. We promote the clinically proven therapeutic advantages of our products and provide quality customer service to physicians and other healthcare providers through our experienced sales and marketing professionals.

Dermatological diseases often persist for an extended period of time and are treated with a variety of clinically proven drugs that are delivered in a variety of formulations. Topical solutions have traditionally included lotions, creams, gels and ointments. These topical delivery systems often inadequately address a patient's needs for efficacy, ease of use and cosmetic elegance, and the failure to address those needs may decrease patient compliance. We believe that VersaFoam®, the proprietary foam delivery system used in OLUX, Luxíq and Evoclin, has significant advantages over conventional therapies for dermatological diseases. The foam formulation liquefies when applied to the skin, and enables the active therapeutic agent to penetrate rapidly. When the foam is applied, it dries quickly and does not leave any residue, stains or odor. We believe that the combination of the increased efficacy and the cosmetic elegance of the foam may actually improve patient compliance and satisfaction. In market research sponsored by Connetics, more than 80% of patients said that they preferred the foam to other topical delivery vehicles.

OLUX and Luxíq compete in the topical steroid market. According to NDC Healthcare, or NDC, for the 12 months ended December 2004, the value of the retail topical steroid market for mid–potency and high– and super–high potency steroids was $869 million. Luxíq competes in the mid–potency steroid market and OLUX competes in the high– and super–high potency steroid market. On March 4, 2004, we acquired from Hoffmann–La Roche, or Roche, the exclusive U.S. rights to Soriatane®, an approved oral therapy for the treatment of severe psoriasis in adults. According to NDC, the value of the entire retail market for psoriasis was $636 million in 2004. In October 2004, we received approval from the Food and Drug Administration, or FDA, for Evoclin for the treatment of acne vulgaris, and we launched Evoclin commercially in December 2004. Evoclin competes in the topical antibiotics market for the treatment of acne. For the 12 months ended December 2004, NDC reported that this market totaled $547 million.

We have one New Drug Application, or NDA, under review by the FDA, and one product candidate in Phase III clinical trials. In August 2004, we submitted an NDA for Velac® (1% clindamycin and 0.025% tretinoin) with the FDA. In October 2004, the FDA accepted the NDA for filing effective as of August 23, 2004 with a user fee goal date of June 25, 2005. In September 2004 we commenced a Phase III clinical trial for Desilux, a low–potency topical steroid for the treatment of atopic dermatitis, formulated with 0.05% desonide in our proprietary emollient foam delivery vehicle, VersaFoam–EF™. In July 2003, we submitted an NDA for Extina® Foam. Extina is an investigational new drug formulation of 2% ketoconazole formulated using our proprietary platform foam delivery vehicle for the treatment of

seborrheic dermatitis. In November 2004, we received a non–approvable letter from the FDA for Extina. The FDA's position was based on the conclusion that, although Extina demonstrated non–inferiority to the comparator drug currently on the market, it did not demonstrate statistically significant superiority to placebo foam. We have continued discussions with the FDA about what, if any, steps we can take to secure approval for Extina, including resubmitting the NDA with additional information or appealing the FDA's decision.

We continue to develop and formulate new product candidates by leveraging the experience and expertise of our wholly owned subsidiary, Connetics Australia Pty Ltd., and the Connetics Center for Skin Biology, or CSB. The CSB, which is a segment of our product development group staffed by Connetics employees, explores ways to optimize drug penetration, distribution, and efficiency at the targeted treatment site on the skin, and assesses novel formulations and new delivery technologies. The CSB assists in the continued development of innovative topical dermatology products through rigorous scientific evaluation of products and product candidates. The CSB presents us with the opportunity to bring together dermatologists and pharmacologists from across the country to interact with our researchers to explore how topical drugs interact with and penetrate the skin. We believe this novel approach to drug development is a key part of our innovation and enables us to bring even more effective and novel treatments to our product platform and the dermatology market. We did not incur any additional costs to establish the CSB, which was created in 2001.

We own worldwide rights to a number of unique topical delivery systems, including several distinctive aerosol foams. We have leveraged our broad range of drug delivery technologies by entering into license agreements with several well–known pharmaceutical companies around the world. Those license agreements for marketed products bear royalties payable to us. In 2001, we entered into a global licensing agreement with Novartis Consumer Health SA for the use of our Liquipatch drug–delivery system in topical antifungal applications. In 2002 we entered into a license agreement with Pfizer, Inc. (formerly Pharmacia Corporation) pursuant to which we granted Pfizer exclusive global rights, excluding Japan, to our proprietary foam drug delivery technology for use with Pfizer's Rogaine® hair loss treatment. In September 2004, we entered into a license agreement granting Pierre Fabre Dermatologie exclusive commercial rights to OLUX for Europe, excluding Italy and the U.K., where the product is licensed to Mipharm S.p.A. The license agreement with Pierre Fabre also grants marketing rights for certain countries in South America and Africa. Pierre Fabre will market the product under different trade names. Under the terms of the license, we will receive an upfront license payment, milestone payments and royalties on product sales. Pierre Fabre will be responsible for costs associated with product manufacturing, sales, marketing, and distribution in its licensed territories. As part of the agreement, we also negotiated a right–of–first–refusal in the United States to an early–stage, innovative dermatology product currently under development by Pierre Fabre. Pierre Fabre anticipates an initial launch of OLUX in select European markets in mid–2005.

OUR STRATEGY

Our principal business objective is to be a leading specialty pharmaceutical company focused on providing innovative treatments in the field of dermatologic disease. To achieve this objective, we intend to continue to pursue our commercial strategy of maximizing product sales by leveraging novel delivery technologies, accelerating the processes of getting products to market, managing the risks of product development where possible, and identifying and targeting specific market opportunities where there are unmet needs. We have described our development paradigm as a "4:2:1 model." We strive in any given year to have four product candidates in product formulation, two product candidates in late–stage clinical trials, and one product or new indication launched commercially. We fuel our product pipeline by a combination of internally developing product candidates and in–licensing novel products that fit with our broader strategy. Key elements of our business and commercialization strategy include the following:

- *Maximizing Commercial Opportunities for OLUX, Luxiq, Soriatane and Evoclin.* We have a focused sales force dedicated to establishing our products as the standard of care for their respective indications. Our commercial strategy is to call on those medical professionals in dermatology who

the drug may cause serious birth defects. Women who are pregnant or might become pregnant during therapy or within three years after stopping therapy should not take Soriatane. Less frequent but potentially serious adverse events that have been reported include liver toxicity, pancreatitis and increased intracranial pressure, as well as bone spurs, alteration in lipid levels, possible cardiovascular effects and eye problems.

Evoclin Foam

Evoclin is a foam formulation of 1% clindamycin for the treatment of acne vulgaris. Evoclin is Connetics' first commercial product that addresses the acne market. According to the National Institute of Arthritis, Musculoskeletal and Skin Disorders, in the U.S. an estimated 17 million people are affected by acne annually, and an estimated 5.6 million people visited a physician for treatment during the 12 months ended October 2004. Prescriptions for the entire topical U.S. acne market in 2004 were approximately $1.2 billion, making it the largest segment of the dermatology market. In the U.S., acne products containing clindamycin generated approximately $416 million in revenue in the 12 month period ended October 2004, making this active ingredient one of the most widely prescribed for acne. Evoclin will compete primarily in the topical antibiotic market, representing approximately $535 million in U.S. prescriptions in the 12 months ended October 2004. We received FDA approval to market Evoclin in October 2004 and began selling the product in December 2004 in 50g and 100g trade unit sizes. Net product revenues for Evoclin for the fourth quarter of 2004 were $2.9 million. Evoclin is indicated for topical application in the treatment of acne vulgaris. Evoclin is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin, a history of regional enteritis or ulcerative colitis, or a history of antibiotic–associated colitis.

PRODUCT CANDIDATES AND CLINICAL TRIALS

Our product candidates require extensive clinical evaluation and clearance by the FDA before we can sell them commercially. Our 4:2:1 development model anticipates that we will conduct simultaneous studies on several products at a given time. However, we regularly re–evaluate our product development efforts. On the basis of these re–evaluations, we have in the past, and may in the future, abandon development efforts for particular products. In addition, any product or technology under development may not result in the successful introduction of a new product.

Extina® Foam

In April 2003, we announced summary results from our Phase III clinical trial with Extina, a foam formulation of a 2% concentration of the antifungal drug ketoconazole for the treatment of seborrheic dermatitis. Ketoconazole is used to treat a variety of fungal infections, including seborrheic dermatitis. Seborrheic dermatitis is a chronic, recurrent skin condition that affects 3–5% of the U.S. population. It usually involves the scalp, but also can affect the skin on other parts of the body, including the face and chest. The symptoms of seborrheic dermatitis include itching, redness and scaling. In 2003 an estimated 1.1 million patients sought physician treatment for seborrheic dermatitis. Extina is intended to compete primarily in the topical antifungal market, representing approximately $752 million in U.S. prescriptions in 2004.

The Extina clinical program consisted of a pivotal trial and two smaller supplemental clinical studies required by the FDA. In the pivotal trial, 619 patients were treated for four weeks in a double–blind, placebo– and active–controlled protocol. As designed, the trial results demonstrated that Extina was not inferior to Nizoral® (ketoconazole) 2% cream as measured by the primary endpoint of Investigator's Static Global Assessment, or ISGA. The trial was also designed to compare Extina to placebo foam per the ISGA. The result, although in favor of Extina, did not achieve statistical significance. On all other endpoints, statistical significance was achieved; therefore, we believe that the totality of the data demonstrated that Extina was clinically superior to placebo foam. In July 2003, we submitted an NDA to the FDA for Extina.

In November 2004, the FDA issued a non–approvable letter for Extina. The FDA's position was based on the conclusion that, although Extina demonstrated non–inferiority to the comparator drug currently on the market, it did not demonstrate statistically significant superiority to placebo foam. We have continued discussions with the FDA about what, if any, steps we can take to secure approval for Extina, including resubmitting the NDA with additional information or appealing the FDA's decision.

Velac®

In December 2002, we initiated the Phase III program for Velac, a first–in–class combination of 1% clindamycin and 0.025% tretinoin, for the treatment of acne. The Velac clinical program consists of two pivotal trials designed to demonstrate superiority to the individual drug products, and two smaller supplemental clinical studies required by the FDA. We completed enrollment of both pivotal trials in late 2003, enrolling over 2,200 patients. In March 2004, we announced the positive outcome of the Phase III clinical trials of Velac. The data from each trial demonstrated a consistently robust and statistically superior treatment effect for Velac compared with clindamycin gel, tretinoin gel and placebo gel on both of the primary endpoints. An analysis of the combined data from the clinical trials demonstrated similar results to the individual trials. The data from these trials also demonstrated that Velac was safe and well tolerated, with the most commonly observed adverse effects being application site reactions such as burning, dryness, redness and peeling. Following this positive clinical outcome, we submitted an NDA with the FDA for Velac in August 2004. The NDA was accepted for filing by the FDA in October 2004 with a filing date of August 23, 2004 and a user fee goal date of June 25, 2005. If approved by the FDA, we believe Velac will compete with topical retinoids as well as topical antibiotics, representing approximately $988 million in U.S. prescriptions during the 12 months ended December 2004. Prescriptions for the entire U.S. acne market during that same period were approximately $1.2 billion not including oral antibiotics.

Desilux™ Foam

In September 2004, we commenced the Phase III clinical program for Desilux, a low–potency topical steroid, formulated with 0.05% desonide in our proprietary emollient foam delivery vehicle. The clinical program focuses on atopic dermatitis and is designed to include infants from three months of age and children up to 17 years old. Subject to a successful Phase III trial outcome, we plan to file an NDA for Desilux in the fourth quarter of 2005.

OLUX–EF

We anticipate initiating Phase III clinical trials for an emollient foam of OLUX, or OLUX–EF, by the end of the first quarter of 2005. OLUX–EF is a super–high potency steroid in our new proprietary ethanol–free emollient VersaFoam vehicle indicated for the treatment of steroid responsive dermatological diseases. Our clinical trials will be conducted in atopic dermatitis and psoriasis.

Other Pipeline Formulations

In addition to the product candidates described above, we are also developing the foam technology for other disease indications. As part of our 4:2:1 development model, we strive to have four product candidates in product formulation at any given time, so that we have some flexibility in determining which two to move into human clinical trials. Our most promising preclinical candidates include an emollient foam of Luxíq , a low potency steroid, as well as other formulation candidates in early stages of development. We are exploring various product formulations for Liquipatch as well, which is described in more detail below under *"Royalty–Bearing Products and Licensed Technology — Liquipatch."*

ROYALTY–BEARING PRODUCTS AND LICENSED TECHNOLOGY

Foam Technology. In 2002 we entered into a license agreement with Pfizer, Inc. (formerly Pharmacia Corporation) pursuant to which we granted Pfizer exclusive global rights, excluding Japan, to our proprietary foam drug delivery technology for use with Pfizer's Rogaine® hair loss treatment. The

We expect that all of our prescription pharmaceutical products will require regulatory approval by governmental agencies before we can commercialize them. The nature and extent of the review process for our potential products will vary depending on the regulatory categorization of particular products. Federal, state, and international regulatory bodies govern or influence, among other things, the testing, manufacture, labeling, storage, record keeping, approval, advertising, and promotion of our products on a product–by–product basis. Failure to comply with applicable requirements can result in, among other things, warning letters, fines, injunctions, penalties, recall or seizure of products, total or partial suspension of production, denial or withdrawal of approval, and criminal prosecution. Accordingly, initial and ongoing regulation by governmental entities in the United States and other countries is a significant factor in the production and marketing of any pharmaceutical products that we have or may develop.

Product development and approval within this regulatory framework, and the subsequent compliance with appropriate federal and foreign statutes and regulations, takes a number of years and involves the expenditure of substantial resources.

FDA Approval. The general process for approval by the FDA is as follows:

- *Preclinical Testing.* Generally, a company must conduct preclinical studies before it can obtain FDA approval for a new therapeutic agent. The basic purpose of preclinical investigation is to gather enough evidence on the potential new agent through laboratory experimentation and animal testing, to determine if it is reasonably safe to begin preliminary trials in humans. The sponsor of these studies submits the results to the FDA as a part of an investigational new drug application, which the FDA must review before human clinical trials of an investigational drug can start. We have filed and will continue to be required to sponsor and file investigational new drug applications, and will be responsible for initiating and overseeing the clinical studies to demonstrate the safety and efficacy that are necessary to obtain FDA approval of our product candidates.

- *Clinical Trials.* Clinical trials are normally done in three distinct phases and generally take two to five years, but may take longer, to complete:
  - Phase I trials generally involve administration of a product to a small number of patients to determine safety, tolerance and the metabolic and pharmacologic actions of the agent in humans and the side effects associated with increasing doses.

  - Phase II trials generally involve administration of a product to a larger group of patients with a particular disease to obtain evidence of the agent's effectiveness against the targeted disease, to further explore risk and side effect issues, and to confirm preliminary data regarding optimal dosage ranges.

  - Phase III trials involve more patients, and often more locations and clinical investigators than the earlier trials. At least one such trial is required for FDA approval to market a branded, or non–generic, drug.

  The rate of completion of our clinical trials depends upon, among other factors, the rate at which patients enroll in the study. Patient enrollment is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the eligibility criteria for the study, and the sometimes seasonal nature of certain dermatological conditions. Delays in planned patient enrollment may result in increased costs and delays, which could have a material adverse effect on our business. In addition, side effects or adverse events that are reported during clinical trials can delay, impede, or prevent marketing approval.
- *Regulatory Submissions.* The Food, Drug and Cosmetic Act outlines the process by which a company can request approval to commercialize a new product. After we complete the clinical trials of a new drug product, we must file an NDA with the FDA. We used the so–called 505(b)(2) application process for OLUX, Luxíq, and Evoclin, which permitted us in each case to satisfy the requirements for a full NDA by relying on published studies or the FDA's findings of safety and effectiveness based on studies in a previously–approved NDA sponsored by another applicant,

together with the studies generated on our products. Generally, although the FDA evaluation of safety and efficacy is the same, the number of clinical trials required to support a 505(b)(2) application, and the amount of information in the application itself, may be substantially less than that required to support a traditional NDA application. The 505(b)(2) process will not be available for all of our other product candidates, and as a result the FDA process may be longer for our future product candidates than it has been for our products to date.

We must receive FDA clearance before we can commercialize any product, and the FDA may not grant approval on a timely basis or at all. The FDA can take between one and two years to review an NDA, and can take longer if significant questions arise during the review process. In addition, if there are changes in FDA policy while we are in product development, we may encounter delays or rejections that we did not anticipate when we submitted the NDA for that product. We may not obtain regulatory approval for any products that we develop, even after committing such time and expenditures to the process. Even if regulatory approval of a product is granted, it may entail limitations on the indicated uses for which the product may be marketed.

Our products will also be subject to foreign regulatory requirements governing human clinical trials, manufacturing and marketing approval for pharmaceutical products. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement are similar, but not identical, to FDA requirements, and they vary widely from country to country.

Manufacturing. The FDA regulates and inspects equipment, facilities, and processes used in the manufacturing of pharmaceutical products before providing approval to market a product. If after receiving clearance from the FDA, we make a material change in manufacturing equipment, location, or process, we may have to undergo additional regulatory review. We must apply to the FDA to change the manufacturer we use to produce any of our products. We and our contract manufacturers must adhere to cGMP and product–specific regulations enforced by the FDA through its facilities inspection program. The FDA also conducts regular, periodic visits to re–inspect equipment, facilities, and processes after the initial approval. If, as a result of these inspections, the FDA determines that our (or our contract manufacturers') equipment, facilities, or processes do not comply with applicable FDA regulations and conditions of product approval, the FDA may seek sanctions and/or remedies against us, including suspension of our manufacturing operations.

Post–Approval Regulation. The FDA continues to review marketed products even after granting regulatory clearances, and if previously unknown problems are discovered or if we fail to comply with the applicable regulatory requirements, the FDA may restrict the marketing of a product or impose the withdrawal of the product from the market, recalls, seizures, injunctions or criminal sanctions. In its regulation of advertising, the FDA from time to time issues correspondence to pharmaceutical companies alleging that some advertising or promotional practices are false, misleading or deceptive. The FDA has the power to impose a wide array of sanctions on companies for such advertising practices.

Pharmacy Boards. We are required in most states to be licensed with the state pharmacy board as either a manufacturer, wholesaler, or wholesale distributor. Many of the states allow exemptions from licensure if our products are distributed through a licensed wholesale distributor. The regulations of each state are different, and the fact that we are licensed in one state does not authorize us to sell our products in other states. Accordingly, we undertake an annual review of our license status and that of SPS to ensure continued compliance with the state pharmacy board requirements.

Fraud and Abuse Regulations. We are subject to various federal and state laws pertaining to health care "fraud and abuse," including anti–kickback laws and false claims laws. The Office of Inspector General, or OIG, of the U.S. Department of Health and Human Services has provided guidance that outlines several considerations for pharmaceutical manufacturers to be aware of in the context of marketing and promotion of products reimbursable by the federal health care programs. Effective July 1, 2005, pursuant to a new California law, all pharmaceutical companies doing business in California will be required to certify that they are in compliance with the OIG guidance.

not have full control over our third–party manufacturers' compliance with these regulations and standards. Our business interruption insurance, which covers the loss of income for up to $14.1 million at our California and Australia locations, and lower amounts for each of our contract manufacturers, may not completely mitigate the harm to our business from the interruption of the manufacturing of products. The loss of a manufacturer could still have a negative effect on our sales, margins and market share, as well as our overall business and financial results.

If our supply of finished products is interrupted, our ability to maintain our inventory levels could suffer and future revenues may be delayed.

We try to maintain inventory levels that are no greater than necessary to meet our current projections. Any interruption in the supply of finished products could hinder our ability to timely distribute finished products. If we are unable to obtain adequate product supplies to satisfy our customers' orders, we may lose those orders and our customers may cancel other orders and stock and sell competing products. This in turn could cause a loss of our market share and negatively affect our revenues.

Supply interruptions may occur and our inventory may not always be adequate. Numerous factors could cause interruptions in the supply of our finished products including shortages in raw material required by our manufacturers, changes in our sources for manufacturing, our failure to timely locate and obtain replacement manufacturers as needed and conditions affecting the cost and availability of raw materials.

We cannot sell our current products and product candidates if we do not obtain and maintain governmental approvals.

Pharmaceutical companies are subject to heavy regulation by a number of national, state and local agencies. Of particular importance is the FDA in the United States. The FDA has jurisdiction over all of our business and administers requirements covering testing, manufacture, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our products. If we fail to comply with applicable regulatory requirements, we could be subject to, among other things, fines, suspensions of regulatory approvals of products, product recalls, delays in product distribution, marketing and sale, and civil or criminal sanctions.

The process of obtaining and maintaining regulatory approvals for pharmaceutical products, and obtaining and maintaining regulatory approvals to market these products for new indications, is lengthy, expensive and uncertain. The manufacturing and marketing of drugs, including our products, are subject to continuing FDA and foreign regulatory review, and later discovery of previously unknown problems with a product, manufacturing process or facility may result in restrictions, including recall or withdrawal of the product from the market. The FDA is permitted to revisit and change its prior determinations and it may change its position with regard to the safety or effectiveness of our products. Even if the FDA approves our products, the FDA is authorized to impose post–marketing requirements such as:

- testing and surveillance to monitor the product and its continued compliance with regulatory requirements,
- submitting products for inspection and, if any inspection reveals that the product is not in compliance, prohibiting the sale of all products from the same lot,
- suspending manufacturing,
- recalling products, and
- withdrawing marketing approval.

Even before any formal regulatory action, we could voluntarily decide to cease distribution and sale or recall any of our products if concerns about safety or effectiveness develop.

To market our products in countries outside of the United States, we and our partners must obtain approvals from foreign regulatory bodies. The foreign regulatory approval process includes all of the risks associated with obtaining FDA approval, and approval by the FDA does not ensure approval by the regulatory authorities of any other country.

In its regulation of advertising, the FDA from time to time issues correspondence to pharmaceutical companies alleging that some advertising or promotional practices are false, misleading or deceptive. The FDA has the power to impose a wide array of sanctions on companies for such advertising practices, and if we were to receive correspondence from the FDA alleging these practices we might be required to:

- incur substantial expenses, including fines, penalties, legal fees and costs to comply with the FDA's requirements,
- change our methods of marketing and selling products,
- take FDA-mandated corrective action, which could include placing advertisements or sending letters to physicians rescinding previous advertisements or promotion, and
- disrupt the distribution of products and stop sales until we are in compliance with the FDA's position.

We may spend a significant amount of money to obtain FDA and other regulatory approvals, which may never be granted. Failure to obtain such regulatory approvals could adversely affect our prospects for future revenue growth.

Successful product development in our industry is highly uncertain, and the process of obtaining FDA and other regulatory approvals is lengthy and expensive. Very few research and development projects produce a commercial product. Product candidates that appear promising in the early phases of development may fail to reach the market for a number of reasons, including that the product candidate did not demonstrate acceptable clinical trial results even though it demonstrated positive preclinical trial results, or that the product candidate was not effective in treating a specified condition or illness.

The FDA approval processes require substantial time, effort and expense. The FDA continues to modify product development guidelines and we may not be able to obtain FDA approval to conduct clinical trials or to manufacture and market any of the products we develop, acquire or license. Clinical trial data can be the subject of differing interpretation, and the FDA has substantial discretion in the approval process. The FDA may not interpret our clinical data the way we do. The FDA may also require additional clinical data to support approval. The FDA can take between one and two years to review new drug applications, or longer if significant questions arise during the review process. Moreover, the costs to obtain approvals could be considerable and the failure to obtain, or delays in obtaining, an approval could have a significant negative effect on our business.

Any factor adversely affecting the prescription volume related to our products could harm our business, financial condition and results of operations.

We derive all of our prescription volume from OLUX, Luxíq, Soriatane and Evoclin. Accordingly, any factor adversely affecting our sales related to these products, individually or collectively, could harm our business, financial condition and results of operations. OLUX, Luxíq and Evoclin are all currently subject to generic competition in their respective markets, and each of them could be rendered obsolete or uneconomical by regulatory or competitive changes. A generic competitor for Soriatane could enter the market at any time which would have a significantly negative impact on its sales. Sales of all of our products could also be adversely affected by other factors, including:

- manufacturing or supply interruptions;
- the development of new competitive pharmaceuticals and technological advances to treat the conditions addressed by our core branded products;

Table of Contents

	Years Ended December 31,				
	2004	2003	2002	2001	2000
	(In thousands, except per share amounts)				
Diluted Earnings Per Share —					
Income (loss) per share before cumulative effect of change in accounting principle	$ 0.51	$ (0.13)	$ (0.54)	$ (0.56)	$ 1.07
Cumulative effect of change in accounting principle, net of tax	—	—	—	—	(0.17)
Net income (loss) per share	$ 0.51	$ (0.13)	$ (0.54)	$ (0.56)	$ 0.90
Shares used to calculate basic net earnings (loss) per share	35,036	31,559	30,757	29,861	28,447
Shares used to calculate diluted net earnings (loss) per share	37,443	31,559	30,757	29,861	30,086
Pro forma amounts assuming the accounting change was applied retroactively:					
Net income (loss)	$ 19,015	$ (4,100)	$ (16,590)	$ (16,742)	$ 32,188
Earnings per share:					
Basic	$ 0.54	$ (0.13)	$ (0.54)	$ (0.56)	$ 1.13
Diluted	$ 0.51	$ (0.13)	$ (0.54)	$ (0.56)	$ 1.07
Consolidated Balance Sheet Data:					
Cash, cash equivalents, marketable securities and restricted cash	$ 76,346	$ 114,966	$ 33,788	$ 48,476	$ 80,184
Working capital	71,094	112,247	25,185	44,026	71,030
Total assets	245,728	145,897	59,553	72,327	85,713
Convertible senior notes	90,000	90,000	—	—	—
Total stockholders' equity	127,920	45,754	44,743	61,354	72,606

(1) In the second quarter of 2003, we received a one-time royalty payment from S.C. Johnson in the amount of $2.9 million in connection with our aerosol spray technology.

(2) In March 2004, we acquired exclusive U.S. rights to Soriatane, resulting in an intangible asset that is being amortized 10 years. Amortization charges for the Soriatane rights in 2004 were $10.6 million.

(3) In May 2002, we entered into an agreement with Yamanouchi Europe, B.V. to license Velac. In connection with this agreement we paid Yamanouchi an initial $2.0 million licensing fee in the second quarter of 2002 and recorded another $2.0 million in the fourth quarter of 2002 when we initiated the Phase III trial for Velac. In the third quarter of 2004, we recorded an additional milestone payment of $3.5 million upon filing an NDA with the FDA.

(4) In 2001, we recorded a net charge of $1.1 million representing costs accrued in connection with the reduction in workforce and the wind down of relaxin development contracts.

(5) In the fourth quarter of 2000, we recorded a $43.0 million gain on the sale of securities.

(6) In April 2001, we sold our rights to Ridaura including inventory to Prometheus Laboratories, Inc. for $9.0 million in cash plus a royalty on annual sales in excess of $4.0 million through March 2006. We recognized a gain of $8.0 million in connection with the sale of Ridaura.

(7) Effective January 1, 2000, we changed our method of accounting for non-refundable license fees in accordance with Staff Accounting Bulletin 101, "Revenue Recognition in Financial Statements."

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion should be read in conjunction with the Consolidated Financial Statements and Notes to Consolidated Financial Statements filed with this Report.

OVERVIEW

Business Overview

We are a specialty pharmaceutical company that develops and commercializes innovative products for the dermatology market. Our products aim to improve the management of dermatological diseases and

CERTAIN EVENTS IN 2004

During 2004, we filed NDA's with the FDA for our product candidates Extina, a foam formulation of a 2% concentration of the antifungal drug ketoconazole, for the treatment of seborrheic dermatitis, and Velac, a combination of 1% clindamycin and 0.025% tretinoin, for the treatment of acne. We also commenced Phase III clinical trials for our product candidate, Desilux, a low–potency topical steroid, formulated with 0.05% desonide in our proprietary emollient foam delivery vehicle.

In February 2004, we completed the sale of 3.0 million shares of our common stock in a private offering to certain accredited investors at a price of $20.25 per share for net proceeds of $56.9 million. We used the proceeds from this offering to acquire the exclusive U.S. rights to Roche's Soriatane, which we completed in March 2004. Including the purchase price of $123.0 million, assumed liabilities of $4.1 million and transaction costs of $529,000, we recorded an intangible asset of approximately $127.7 million related to the Soriatane acquisition, which we are amortizing over an estimated useful life of 10 years. In July 2004, we entered into a multi–year consent with Roche to sell Soriatane to a U.S.–based distributor that exports branded pharmaceutical products to select international markets. Product sold to this distributor is not permitted to be resold in the U.S. Under the terms of the agreement, we will pay a royalty to Roche on Soriatane sales made during the term of the agreement to this distributor.

In March 2004, we entered into an agreement with UCB Pharma, a subsidiary of UCB Group, pursuant to which we authorized UCB Pharma to promote OLUX and Luxíq to a segment of U.S. PCP's. In September 2004, in connection with UCB Pharma's acquisition of Celltech plc, UCB notified us that it intended to discontinue the co–promotion agreement, effective March 31, 2005. UCB will continue to promote OLUX and Luxíq until then. Through the end of the promotion period, UCB's focus will be on approximately 10% of PCP's who are active prescribers of dermatology products, including OLUX and Luxíq. The purpose of the co–promotion agreement is to ensure appropriate use of OLUX and Luxíq with the current PCP users and to build value for the OLUX and Luxíq brands. We estimate that before we entered into the agreement with UCB Pharma, PCP's wrote approximately 15% of prescriptions for OLUX and Luxíq, even though we have promoted primarily to dermatologists. We pay UCB a fee based on prescriptions written by targeted PCP's which is recorded as an expense in selling general and administrative expense. UCB bears the marketing costs for promoting the products (including product samples, marketing materials, etc.). We will not have any financial obligation to UCB on prescriptions generated by PCP's after March 31, 2005.

In August 2004, we submitted an NDA for Velac (1% clindamycin and 0.025% tretinoin) with the FDA and, in October 2004, we received notification that the FDA accepted the NDA for filing as of August 23, 2004. For the three months ended September 30, 2004, we recorded a $3.5 million fee due to the licensor upon the filing of the NDA. Because the product has not been approved and has no alternative future use, we recorded the fee as an in–process research and development and milestone expense. Under the terms of the license agreement we entered into in 2002 with Yamanouchi Europe B.V., we hold exclusive rights to develop and commercialize Velac in the U.S. and Canada and non–exclusive rights in Mexico.

In September 2004, we licensed to Pierre Fabre Dermatologie exclusive commercial rights to OLUX for Europe, excluding Italy and the U.K. where the product is licensed to Mipharm S.p.A. The license agreement with Pierre Fabre also grants marketing rights for certain countries in South America and Africa. Pierre Fabre will market the product under different trade names. Under the terms of the license, we received an upfront license payment of $250,000 and we will receive milestone payments and royalties on product sales. Pierre Fabre will be responsible for costs associated with product manufacturing, sales, marketing and distribution in its licensed territories. As part of the agreement, we also negotiated a right–of–first–refusal in the U.S. to an early–stage, innovative dermatology product currently under development by Pierre Fabre. Pierre Fabre anticipates an initial launch of OLUX in select European markets in mid–2005.

In October 2004, we received approval from the FDA for Evoclin (clindamycin) Foam, 1% for the treatment of acne vulgaris. Evoclin is delivered in our proprietary VersaFoam vehicle. In anticipation of the commercial launch of Evoclin, we hired 66 sales professionals in November 2004 and we announced the commercial launch of the product in December 2004 with the availability of 50g and 100g trade unit sizes.

In November 2004, the FDA notified us that it would not approve Extina. The FDA's position was based on the conclusion that, although Extina demonstrated non–inferiority to the comparator drug currently on the market, it did not demonstrate statistically significant superiority to placebo foam. We have continued discussions with the FDA about what, if any, steps we can take to secure approval for Extina.

In November 2004 we announced that Medicis informed us that it has in–licensed rights to an issued patent that it asserts will be infringed by our product candidate Velac. Based on our prior review of the Medicis licensed patent, we believe that Velac will not infringe the patent assuming the patent is valid. While we are not aware of any legal filings related to this assertion by the patent holder or Medicis, we believe, based on information publicly available on the USPTO website, that the inventor named on the patent has filed a Reissue Patent Application with the USPTO. To our knowledge, the USPTO has not formally announced the filing of the reissue application in the Official Gazette as of the date of this Report.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States, or GAAP. These accounting principles require us to make certain estimates, judgments and assumptions. We believe that the estimates, judgments and assumptions upon which we rely are reasonable based upon information available to us at the time that they are made. These estimates, judgments and assumptions can affect the reported amounts of assets and liabilities as of the date of the financial statements, as well as the reported amounts of revenues and expenses during the periods presented. To the extent there are material differences between these estimates, judgments or assumptions and actual results, our financial statements will be affected.

Our senior management has reviewed these critical accounting policies and related disclosures with our Audit Committee. Our significant accounting policies are described in Note 2 to the Consolidated Financial Statements included in this Report. We believe the following critical accounting policies affect our more significant judgments, assumptions, and estimates used in the preparation of our condensed consolidated financial statements, and therefore are important in understanding our financial condition and results of operations.

Revenue Recognition — Reserves for Discounts, Returns, Rebates and Chargebacks.

We recognize product revenue net of allowances for estimated discounts, returns, rebates and chargebacks. We allow a discount for prompt payment. We estimate these allowances based primarily on our past experience. We also consider the volume and price mix of products in the retail channel, trends in distributor inventory, economic trends that might impact patient demand for our products (including competitive environment), and other factors.

We accept from customers the return of pharmaceuticals that are within six months before their expiration date. As a practice, we avoid shipping product that has less than ten months dating. We authorize returns for damaged products and exchanges for expired products in accordance with our returned goods policy and procedures. We monitor inventories in the distributor channel to help us assess the rate of return.

We establish and monitor reserves for rebates payable by us to managed care organizations and state Medicaid programs. Generally, we pay managed care organizations and state Medicaid programs a rebate on the prescriptions filled that are covered by the respective programs with us. We determine the reserve

amount at the time of the sale based on our best estimate of the expected prescription fill rate to managed care and state Medicaid patients, adjusted to reflect historical experience and known changes in the factors that impact such reserves.

In the past, actual discounts, returns, rebates and chargebacks have not generally exceeded our reserves. However, the rates and amount in future periods are inherently uncertain. Our revenue reserve rate was approximately 17% of our gross product revenues for 2004 compared to 14% in 2003, reflecting the higher reserve requirements for Soriatane. If future rates and amounts are significantly greater than the reserves we have established, the actual results would decrease our reported revenue; conversely, if actual returns, rebates and chargebacks are significantly less than our reserves, this would increase our reported revenue. If we changed our assumptions and estimates, our revenue reserves would change, which would impact the net revenue we report.

Goodwill, Purchased Intangibles and Other Long–Lived Assets — Impairment Assessments

We have in the past made acquisitions of products and businesses that include goodwill, license agreements, product rights, and other identifiable intangible assets. We assess goodwill for impairment in accordance with Statement of Financial Accounting Standards No. 142, *"Goodwill and other Intangible Assets,"* or SFAS 142, which requires that goodwill be tested for impairment at the "reporting unit level" ("reporting unit") at least annually and more frequently upon the occurrence of certain events, as defined by SFAS 142. Consistent with our determination that we have only one reporting segment, we have determined that there is only one reporting unit, specifically the sale of specialty pharmaceutical products for dermatological diseases. We test goodwill for impairment in the annual impairment test on October 1 using the two–step process required by SFAS 142. First, we review the carrying amount of the reporting unit compared to the "fair value" of the reporting unit based on quoted market prices of our common stock and on discounted cash flows based on analyses prepared by management. An excess carrying value compared to fair value would indicate that goodwill may be impaired. Second, if we determine that goodwill may be impaired, then we compare the "implied fair value" of the goodwill, as defined by SFAS 142, to its carrying amount to determine the impairment loss, if any. Based on these estimates, we determined that as of October 1, 2004 there was no impairment of goodwill. Since October 1, 2004, there have been no indications of impairment and the next annual impairment test will occur as of October 1, 2005.

In accordance with Statement of Financial Accounting Standards No. 144, *"Accounting for Impairment or Disposal of Long–Lived Assets,"* or SFAS 144, we evaluate purchased intangibles and other long–lived assets, other than goodwill, for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable based on expected undiscounted cash flows attributable to that asset. The amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. We have not recorded any impairment charges for long–lived intangible assets for the three years ended December 31, 2004.

Assumptions and estimates about future values and remaining useful lives are complex and often subjective. They can be affected by a variety of factors, including external factors such as industry and economic trends, and internal factors such as changes in our business strategy and our internal forecasts. Although we believe the assumptions and estimates we have made in the past have been reasonable and appropriate, different assumptions and estimates could materially impact our reported financial results. Accordingly, future changes in market capitalization or estimates used in discounted cash flows analyses could result in significantly different fair values of the reporting unit, which may result in impairment of goodwill.

Income Taxes

We recognize deferred tax assets and liabilities for temporary differences between the financial reporting basis and the tax basis of our assets and liabilities. We record valuation allowances against our

Table of Contents

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Connetics Corporation
a Delaware corporation
By: /s/ John L. Higgins

John L. Higgins
Chief Financial Officer
Executive Vice President, Finance and Corporate Development

Date: March 15, 2005

Each person whose signature appears below constitutes and appoints Katrina J. Church and John L. Higgins, jointly and severally, his or her attorneys–in–fact and agents, each with the power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10–K, and to file the same, with exhibits and other documents in connection therewith, with the Securities and Exchange Commission, granting to each attorney–in–fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully as he or she might or could do in person, and ratifying and confirming all that the attorneys–in–fact and agents, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
Principal Executive Officer:		
/s/ Thomas G. Wiggans Thomas G. Wiggans	Chief Executive Officer and Director	March 15, 2005
Principal Financial and Principal Accounting Officer:		
/s/ John L. Higgins John L. Higgins	Chief Financial Officer; Executive Vice President, Finance and Corporate Development	March 15, 2005
Directors:		
/s/ Alexander E. Barkas Alexander E. Barkas	Director	March 15, 2005
/s/ Eugene A. Bauer Eugene A. Bauer	Director	March 15, 2005

Table of Contents

Signature	Title	Date
/s/ R. Andrew Eckert R. Andrew Eckert	Director	March 15, 2005
/s/ Denise M. Gilbert Denise M. Gilbert	Director	March 15, 2005
/s/ John C. Kane John C. Kane	Director	March 15, 2005
/s/ Thomas D. Kiley Thomas D. Kiley	Director	March 15, 2005
/s/ Leon E. Panetta Leon E. Panetta	Director	March 15, 2005
/s/ G. Kirk Raab G. Kirk Raab	Chairman of the Board	March 15, 2005